the right to pursue the same or similar subject matter in a continuing application or other related application. Applicants submit that the amendments to the claims are made solely to clarify that which applicants regard as their invention and not to overcome the cited prior art.

Support for the claims is found throughout the specification, therefore, the amended claims do not constitute new subject matter. Specifically, support can be found for the claims, for example, in the following pages and lines of the present specification: Section II.C. Preparation of Antigenic Polypeptides and Conjugation with Carrier - page 47, line 24 through page 53, line 36; Section II.D. Preparation of Hybrid Particle Immunogens Containing HCV Epitopes - page 54, line 1 through page 55, line 3; Section II.E. Preparation of Vaccines - page 55, line 5 through page 58, line 29; Section II.F. Dosage and Administration of Vaccines - page 58, line 31 through page 59, line 21; Section II.G. Preparation of Antibodies Against HCV Epitopes - page 59, line 23 through page 61, line 2.

35 U.S.C. § 112, 2nd Paragraph Rejections:

Claims 88 is rejected under 35 U.S.C. § 112, second paragraph as indefinite with respect to the terms "substantially isolated" and "polypeptide... of an envelope domain of an HCV genome..." Applicants submit that claim 88 has been amended to replace "substantially isolated" with "isolated" and to replace "...domain of an HCV genome..." with "...domain encoded by an HCV genome...," therefore render the rejections over the terms moot.

Claim 105 is rejected as being incomplete. Claim 105 has been canceled, and the subject matter of claim 105 has been encompassed within claim 106. As such, Applicants respectfully request the §112, second paragraph rejection over claim 105 be withdrawn.

Claims 92-95 are rejected as improperly dependent from claim 88 because there is allegedly insufficient antecedent basis for core, NS1 and NS2 regions in the independent claim 88. Applicants respectfully traverse the rejection and supporting remarks. Applicants first point out that claims 93-95 are not dependent claims. They are independent claims directed to different immunogenic compositions comprising immunogenic HCV polypeptides from the core, NS1 or NS2 regions, respectively. With respect to claim 92, which is a claim dependent from

claim 88, the claim is directed to a composition of claim 88 further comprising additional immunogenic HCV polypeptide from the core region and immunogenic fragments thereof. Thus, the additional core region polypeptide does not need to be included in the Markush group of claim 88.

Claims 88, 92-96 and 104 are also rejected for reciting "immunogenic polypeptide or fragments" of various HCV proteins. It is alleged that the metes and bounds of the term "fragments" of a polypeptides are unclear, and a fragment could be one amino acid which would be unlikely immunogenic. Applicants respectfully traverse this rejection. The claims recite "... immunogenic HCV polypeptide ... and immunogenic fragments of said polypeptide...." Therefore, the term "immunogenic fragments" of the claims is directed to fragments of the HCV polypeptides that retain the immunogenicity with respect to HCV, whether alone or in the presence of a carrier and/or adjuvant, and thus do not encompass any and all polypeptides or fragments that are not immunogenic with respect to HCV.

Applicants submit that the claims as amended are in compliance with the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, applicants respectively request that the Examiner withdraw the rejections under 35 U.S.C. § 112, second paragraph.

35 U.S.C. § 112, 1st Paragraph Rejections:

a. Claims 89-91 with respect to "E1, E1 and E1/E2 complex"

Claims 89-91 were rejected under 35 U.S.C. § 112, first paragraph because the specification allegedly lacks written description for "E1 domain, E2 domain, or E1/E2 aggregate of HCV." Applicants respectfully traverse the rejection and its supporting remarks.

Applicants point out that literal support for specific viral polypeptide domains can be found throughout the specification. For example, section II.J. at page 74 teaches the identification and localization of specific viral polypeptide antigens such as coat or envelope antigens, or internal antigens such as nucleic acid binding proteins, core antigens.... II.E. describes HCV vaccines comprising one or more epitopes from one or more structural proteins,

and/or one or more epitopes from one or more nonstructural proteins. Particularly preferred are vaccines comprising E and/or NS1, or subunits thereof (page 56, lines 7-17). Descriptions of the envelope region of HCV, including EnvL and EnvR, and their use can be found in the specification at, *inter alia*, Example IV.H.7.b. and Fig. 85A. For example, the specification at page 210, lines 24-31 teaches that the "EnvL" region encompasses nucleotides 669-1243, and putative amino acids 117 to 308; the "EnvR" region encompasses nucleotides 1215-1629, and encodes putative amino acids 300-408. On pages 213 to 214, sequence information on variants in the EnvL and EnvR regions obtained from different HCV isolates are compared for their homology. Accordingly, adequate disclosure can be found in the specification supporting claims 89-91. Applicants respectfully request the written description rejection over claims 89-91 under §112, first paragraph be withdrawn.

b. The Enablement Rejection of Claims 88-114

Claims 88-114 were rejected under 35 U.S.C. § 112, first paragraph, because the specification is alleged as not enabling with respect to immunogenic HCV polypeptides or immunogenic fragments thereof, and methods of using those compositions to provoke an immune response. Applicants respectfully traverse this rejection and its supporting remarks.

35 U.S.C. §112 ¶1 requires a patent to contain a description that enables one skilled in the art to make and use the claimed invention. *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 f.2D 1569, 1576 (Fed. Cir. 1984). An enabling specification may asume familiarity with prior art that is well known to those of skill in the art. *Lindemann Masachinenfabrik GMNH v. Am Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984). Nothing more than objective enablement is required, and therefore it is irrelevant how such a teaching is provided, either by broad terminology or by illustrative examples. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Marzocchi*, 169 USPQ 367, 369 (CCPA, 1971). That some experimentation is necessary does not constitute a lack of enablement; the amount of experimentation, however, must not be unduly extensive. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) According to the Court, "the key word is '**undue**,' not experimentation." *Wands* at 1404 (emphasis added). Furthermore, the determination of what constitutes undue experimentation in a given case

requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. *Id.*

What is at issue is whether the specification provides enough guidance as to how to identify immunogenic polypeptides of HCV such that they could be tested in such a known manner. (Cf. Paper 16, page 6.) The Action acknowledges that the specification details the production of several antigenic polypeptides and many potential antigenic sequences (Paper 16, page 5), and that the specification devotes much description to the definition of an antigenic polypeptide, how it is identified, and examples of antigenic polypeptides (Paper 16, page 6). Also acknowledged is that methods of testing a polypeptide for immunogenicity were known in the art at the time of the invention (Paper 16, page 6).

However, it is asserted in the Action that the immunogenicity of the antigenic polypeptides is not discussed, that the specification does not set forth defining characteristics that must be present in a polypeptide for it to be immunogenic, and that it does not point to examples of immunogenic HCV sequences. Moreover, it is asserted that the specification does not draw a link between a polypeptide's antigenicity and immunogenicity. These assertions are erroneous.

It is known in the art that antigenicity and immunogenicity are correlated properties of a molecule of interest. In "Cambridge Directory of Biology" (Cambridge, 1989), for example, "antigen" is defined as "a substance which has determinant groups which can interact with specific receptors on lymphocytes or on antibodies. The term is often used to include substances which can stimulate an immune response, although these are more correctly termed *immunogen.*" (A copy of the relevant page is attached herein.) Moreover, Dr. Weiner, in a Declaration previously submitted in this case on November 16, 1998, stated that it is well known to those of skilled in the art that antigenicity reflects the immunogenicity of a polypeptide region (Weiner Declaration, ¶5). No evidence has been provided to refute Dr. Weiner's statement.

The correlation between antigenicity and immunogenicity is presented in the specification. In the Examples, the antigenicity of isolated HCV polypeptides was tested by direct immunological screening using sera obtained HCV infected individuals. (See, for

example, IV.B.8. "Expression and Antigenicity of Polypeptides Encoded in HCV cDNA" at pages 149-153.) One of ordinary skill in the art would know that the antibodies in this sera resulted from the immunogenicity of the viral antigens, and that the antigenic regions of the isolated polypeptides that bound the anti-HCV antibodies must duplicate the regions that were immunogenic *in vivo*. This correlation between antigenicity and immunogenicity is found, *inter alia*, in Section IV.B.8.a. A segment of this section states the following:

> "As seen from the test results shown in FIG. 65, a number of clones expressed polypeptides containing HCV epitopes which were immunologically reactive with serum from individuals with NANBH. Five of these polypeptides were very ***immunogenic*** in that antibodies to HCV epitopes in these polypeptides were detected in many different patient sera. The clones encoding these polypeptides, and the location of the polypeptide in the putative HCV polyprotein (wherein the amino acid numbers begin with the putative initiator codon) are the following: clone 5-1-1, amino acids 1694-1735; clone C100, amino acids 1569-1931; clone 33c, amino acids 1192-1457; clone CA279a, amino acids 1-84; and clone CA290a amino acids 9-177. The ***location*** of the ***immunogenic polypeptides within the putative HCV polyprotein*** are shown immediately below....[table listing clones encoding polypeptides of proven reactivity within sera from NANBH patients, and the location of the encoded amino acid sequences within an HCV polyprotein].
>
> The results on the ***immunogenicity*** of the polypeptides encoded in the various clones examined suggest efficient detection and immunization systems may include panels of HCV polypeptides/epitopes." (Page 150, line 31 to page 153, line 4; emphasis added)

Applicants point out that the table within the above-referenced paragraph on page 152 provides examples of clones located in the particular HCV regions as recited in the pending claims, and theses clones encode polypeptides of proven reactivity with sera from NANBH patients. For example, according to the table bridging pages 147 and 148, the CA279a clone (AA1-84) is located within the core region (AA1-120); the CA74a clone (AA437-582) is located within the NS1 region (AA400-660); 13i clone (AA511-690) is located within the NS1-NS2 regions (AA400-1050); and CA290a (AA9-177) is within the core and envelope regions (AA1-400). Some of these clones, such as CA279a and CA290a encode polypeptides that "were very immunogenic...." (page 150, line 34 to page 151, line 7).

Moreover, the specification provides a list of HCV polypeptides that "comprise an epitope or ***are immunogenic***" with respect to HCV (pages 51-52). The 188 HCV polypeptides of various length listed therein span the entire HCV polyprotein, including the particular regions recited in the claims--i.e., the envelope, core, NS1 and NS2 regions. (Compare the list with the table bridging pages 147 and 148, wherein the approximate boundaries for putative domains are listed).

As mentioned above, it is acknowledged in the Action that the production and identification of polypeptides that are antigenic for HCV is taught and enabled within the instant specification[1]. The specification further provides teachings on how to make and use compositions that are immunogenic with respect to HCV comprising the antigenic HCV polypeptides. Applicants particularly point to sections II.B.--II.F., wherein the preparation and use of various immunogenic compositions comprising antigenic HCV polypeptides are described at great length.

Section II.B. describes the preparation of antigenic HCV polypeptides. Section II.C., titled "Preparation of Antigenic Polypeptides and Conjugation with Carrier", precisely teaches how to make an isolated antigenic polypeptide immunogenic. The section begins by pointing out the fact that an antigenic region of a polypeptide is generally relatively small--typically 8 to 10 amino acids or less in length. In the instances the HCV polypeptide is correctly configured so as

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[1] As attested by Dr. Chien in his Declaration originally filed on December 13, 1995 in the prosecution of related case U.S.S.N. 08/306,472 (later issued as U.S. Patent 5,698,390), a copy of which is submitted herein with this response, at least 150 of the 188 polypeptides listed on page 51 and 52 contain antigenic regions that were identifiable by immunological screening with human anti-HCV antisera.[1] (See, Chien Declaration ¶ 11.)

The technique used by Dr. Chien to identify the antigenic 8-mer polypeptides that were bound by infected sera from HCV infected individuals, PEPSCAN, was available and known to those of ordinary skill in the art as of November 18, 1987 (the date of filing of the first priority parent application). Utilizing this technique and the HCV sequence information provided in the present application, nearly 500 discrete polypeptides were identified that bind antibodies in the sera from HCV infected individuals; the identified polypeptides span the entire HCV polyprotein (Chien Declaration, Exhibit D). Dr. Chien states that the vast majority of these would be functional antigens for anti-HCV antibodies (Chien Declaration, ¶ 9). Dr. Chien accomplished these screening results within three weeks utilizing serum from only 3 infected individuals (Chien Declaration, ¶).

to provide the correct epitope, but is ***too small to be immunogenic, the polypeptide may be linked to a suitable carrier*** (page 47, line 26-page 48, line 3; emphasis added). The section then goes on to teach a number of techniques known in the art for obtaining the linkages (page 48, lines 4-30); and suitable carriers to be used (page 48, line 31-page 49, line 7).

Section II.D describes a system that can be used to enhance the immunogenicity of HCV antigenic regions by preparing them in mammalian or yeast systems fused with or assembled with particle-forming proteins.

Section II.E. lists adjuvants that can be utilized with immunogenic polypeptides.

Section II.G. describes methods for producing antibodies using the immunogenic polypeptides prepared as described in the earlier sections. These antibodies can be monoclonal or polyclonal.

As part of the argument against enablement, the Action provides the unsupported assertion that, "An antigen is not necessarily immunogenic. The ability to be bound by a particular antibody or patient sera is not necessarily predictive of its ability to provoke an immune response." (Paper 16, page 5). In the present circumstances this assertion is erroneous for the following reasons: (1) the Action has stated that Sections II B and II C of the specification "are entirely devoted to 'antigenic' polypeptide production and linkage to a carrier (Paper 16, page 5); (2) an "***immunogenic polypeptide***" is defined as one that elicits a cellular and/or humoral immune response, whether alone ***or linked to a carrier*** in the ***presence or absence of an adjuvant***; (page 35, lines 1-4) and (3) the Action has stated that, ***"Virtually any polypeptide linked to a carrier in the presence of an adjuvant will elicit either a cellular or humoral immune response.....One of ordinary skill in the art might well envision an implied limitation that the response be specific for the polypeptide...."*** (Paper 16, page 5). Thus, the argument to support the lack of enablement rejection contradicts the Office's own assertions on the expected immunogenicity of HCV antigenic polypeptides.

With respect to the Examiner's remarks regarding the specificity of the immunogenic polypeptides as claimed, Applicants point out that the claims are directed to immunogenic HCV

polypeptides of particular regions (i.e., envelop, core, NS1 and NS2), thus defining the specificity of immunogenicity with respect to particular HCV regions. Applicants also point out that the arguments made in the earlier response (November 17, 1998, at page 9) are not inconsistent with the notion of specificity. There Applicants simply stated that the claimed composition, while immunogenic with respect to HCV, does not have to be monospecific--i.e., cross-reactivity with other anti-flavivirus antibodies is possible, and sometimes may be even more desired, within the embodiment of the invention as claimed.

The Action also contends that Section II.E., which discusses immunogenic polypeptides does not refer to any particular regions, sequences or areas of HCV which would be immunogenic, and that the entire section is prophetic in nature. However, as discussed above, the specification does describe particular HCV regions and polypeptides that are immunogenic (for example, in Section IV.B.8.a. and on pages 51 and 52). The specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 164 USPQ 643, 645 (CCPA 1970). The Patent Office's own policy also echoes the established patent law by stating that an example may be "working" or "prophetic;" and that the lack of working examples or lack of evidence that the claimed invention works should never be the sole reason for rejecting the claimed invention on the grounds of lack of enablement. MPEP 2164.02.

Applicants submit that by following the specification, one of ordinary skill in the art could readily prepare and identify without undue experimentation the claimed immunogenic compositions comprising isolated immunogenic HCV polypeptides of particular regions or immunogenic fragments thereof. As such, the claimed invention is enabled under 35 U.S.C. §112 ¶1.

Applicants contend that a *prima facie* case for lack of enablement under 35 U.S.C. §112 ¶1 has not been made by the Office. It is incumbent upon the Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure, and to back up these assertions of its own with acceptable and specific evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, supra, 370 (CCPA 1971). While references supporting a

prima facie case of lack of enablement are preferred but not required, "specific technical reasons are always required." MPEP at 2164.04. If the enablement rejection and the written description requirement rejection discussed below are to be maintained, Applicants respectfully request that the Examiner provide specific support for the allegation that the compositions comprising antigenic HCV polypeptides as taught in the specification, including those designated as immunogenic, would not be immunogenic with respect to HCV. This support can be in the form of either publications or if based upon facts within the personal knowledge of the Examiner, an Examiner's affidavit under 37 CFR §1.104(d)(2). Otherwise, "there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, supra at 370.

c. Written Description Regarding "Immunogenic HCV Polypeptides"

The Office Action alleges that the specification does not offer a written description of any immunogenic polypeptides of HCV, or immunogenic fragments thereof. Reliance for this rejection is based upon the assertion that, "Legal precedent dictates that conception of a chemical compound, such as a DNA molecule, or polypeptide sequence, is not achieved until reduction to practice has occurred [citing *Amgen* and *Fiers*]. At no point in the specification are particular immunogenic polypeptides or immunogenic fragments of HCV polypeptides disclosed." Applicants respectfully traverse this rejection and its supporting remarks.

To fulfill the written description requirement under §112, first paragraph, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention as of the filing date. *Lockwood v. American Airlines, Inc.*, 41 USPQ2d 1961, 1966 (CAFC 1997). Thus, an applicant complies with the written description requirement by describing the invention, with all its claimed limitation, not that which makes it obvious, and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *University of California vs. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404 (CAFC 1997; citing *Lockwood*).

In both *Amgen* (18 USPQ2d, 1016 (CAFC 1991)) and *Fiers* (25 USPQ2d, 1601 (CAFC 1993)), the issue was whether it was sufficient to conceive a DNA by virtue of its functional properties alone. The inventor in either case sought to claim a gene by the functionality of the protein encoded therein (in *Amgen* it is a human erythropoetin; in *Fiers* it is a human fibroblast beta-interferon), without having actually isolated the gene and without being in possession of the gene's sequence information. The court in both cases held, in essence, that conception of a chemical compound including a gene does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its methods of preparation, its physical or chemical properties, or ***whatever characteristics sufficiently distinguish it from other materials, as well as a method for obtaining it***. See, for example, *Amgen* at 1021 (emphasis added). Moreover, a written description also requires the same degree of specificity, as one cannot describe what one has not conceived. *Fiers* at 1606.

Unlike *Amgen* or *Fiers*, the immunogenic compositions are not claimed merely by virtue of functional properties. As stated in the previous responses to Office Actions, the inventors of the present invention for the first time in the long history of hepatitis research successfully isolated cDNA clones encoding HCV--the causative agent of NANBH, and disclosed the entire cDNA sequence of HCV and produced recombinant HCV polypeptides. Therefore, the chemical and genetic structure of the molecules underlying the subject matter being claimed were indeed obtained by the inventors, and HCV polynucleotides and polypeptides were successfully made.

Furthermore, the specification does address the immunogenicity of polypeptides from the disclosed HCV sequences. Section IV.B.8.a. (pages 147 through 153) and pages 51 and 52 delineate a number of polypeptides spanning the core, envelope, NS1 or NS2 regions that are HCV ***immunogenic***. Particularly, Applicants point out that the table on page 152 provides examples of clones located in the particular HCV regions as recited in the pending claims, and theses clones encode polypeptides of proven reactivity with sera from NANBH patients. For example, according to the table bridging pages 147 and 148, the CA279a clone (AA1-84) is located within the core region (AA1-120); the CA74a clone (AA437-582) is located within the NS1 region (AA400-660); 13i clone (AA511-690) is located within the NS1-NS2 regions

(AA400-1050); and CA290a (AA9-177) is within the core and envelope regions (AA1-400). Some of these clones, such as CA279a and CA290a encode polypeptides that "were very immunogenic...." (page 150, line 34 to page 151, line 7).

Thus, one of ordinary skill in the art can clearly conclude that the Applicants invented the claimed invention as of the filing date, and also could readily predict the immunogenicity of HCV proteins from the specification. (See above-discussed reasons as to why the specification is enabling for immunogenic HCV polypeptides.) In *In re Alton,* 37 USPQ2d 1578 (CAFC 1996), the court stated that the adequate written description requirement serves "to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; ***how the specification accomplishes this is not material.***" *Id* at 1581 (emphasis added).

The Action has further comments under the written description rejection that are either erroneous and/or superfluous to the written description requirement. These comments and Applicants responses to them are the following.

On page 9 of the Action, it says that "one is not taught how to use any fragment made." This statement is in error. Section II.E. teaches how to use one or more immunogenic polypeptides derived from HCV to prepare HCV vaccines; and section II.G. in combination with other sections of the specification teaches one of skill in the art how to use the claimed immunogenic compositions to prepare antibodies, both polyclonal and monoclonal.

On page 9 of the Action, it says that "having in hand immunogenic polypeptides permits one to test for those which could confer protective immunity, however, there is no predictability as to which one, if any will elicit protective immunity." Applicants contend that the claimed compositions need not confer protective immunity to be immunogenic--all that is required is that the polypeptide elicits a cellular and/or humoral immune response, whether alone or linked to a carrier in the presence or absence of an adjuvant. It has already been conceded that under these conditions all of the antigenic HCV polypeptides will be immunogenic. ("Virtually any

polypeptide linked to a carrier in the presence of an adjuvant will elicit either a cellular or humoral immune response....")(Paper 16, page 5.)

On page 9 of the Action, it says that "nowhere in the specification are the proteins of HCV described or isolated." Applicants submit that this statement is clearly erroneous. The specification describes HCV polyproteins encoded within HCV genomes; it also describes a multitude of antigenic and immunogenic polypeptides encoded within an HCV genome. Examples in section IV.B. describes expression and purification of polypeptides encoded by various HCV cDNA constructs, including for example, 5-1-1, 81, C100, C33c and C200-C100. Also described are yeast and bacteria systems used for polypeptide expression.

Also on page 9 of the Action, it says that "the claims embrace the proteins which naturally occur as part of the virion, however, the specification fails to set forth their isolation as well as failing to set forth how to isolate the virus. Nor can one infer what proteins are present in the virion from the presumptive polyprotein of HCV as HCV is neither a flavivirus or a togavirus." Applicants contend that the Office is placing requirements that are superfluous to the written description requirement. As discussed above, the specification clearly teaches the structure of antigenic polypeptides present in the immunogenic as claimed, and methods of preparing these compositions. Nowhere does the written description requirement under 35 USC §112 ¶1 require that the specification teach *every* polypeptide that could be immunogenic nor *every* method of preparing the claimed immunogenic compositions.

For all of the above-stated reasons, Applicants contend that the claims meet the requirements for enablement and written description under 35 U.S.C. § 112 ¶ 1 and request that the objections to the specifications and the rejections under this paragraph be withdrawn.

35 U.S.C. § 102 Rejections:

Claims 88-99 and 111-114 remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Bradley, J. Virol. Meth. (1985) 10: 307-309 (referred to hereinafter as "Bradley"); He et al., J. Infect. Dis. (1987) 136(4):636-640 (referred to hereinafter as "He"); and Prince et al.

J. Med. Virol. (1985) 16:119-125 (referred to hereinafter as "Prince"). Applicants respectfully traverse the rejections and their supporting remarks.

In order to anticipate the claims under 35 USC §102(b) each cited publication must disclose each and every limitation within the rejected claims. The cited publications fail to meet this requirement.

All three references, Bradley, He and Prince, reflect research prior to the molecular identification of HCV--including its genome sequence and protein domains--by Applicants of the present invention. The references are directed to intact virus or viruses that had long been suspected as causing non-A non-B hepatitis. As argued previously and attested by Dr. Weiner in her Declaration at ¶13, the NANBV disclosed in the cited references is not necessarily an HCV. Indeed, there are many agents associated with NANBH, including Hepatitis Viruses E, F, G, and newly discovered causative agent of blood-borne hepatitis, S.E.N.-v. To be anticipating under §102, the prior art must sufficiently describe the claimed invention to have placed the public in possession of it. *In re Sasse*, 207 USPQ 107, 111 (CCPA 1980). The three cited references certainly failed to show to the public that the disclosed NANBV was indeed an HCV.

Even if, *arguendo*, the NANBVs of the cited references were HCV strains, the teachings of the references are limited to the pathogenic features of the NANBH disease and associated whole virus agents; and they do not provide any direction as to the molecular and genetic identity of the virus genome, let alone an immunogenic composition comprising an isolated immunogenic viral polypeptide encoded by a particular domain of the viral genome and immunogenic fragments of said polypeptide.

The Examiner suggests that the language of the claims being rejected (pending claims 88-99, and 111-114) reads on intact partially purified virus, which is presumably the basis for the 102(b) rejections over the cited references. Applicants submit that the claims as amended are drawn to immunogenic compositions comprising an isolated immunogenic hepatitis C virus (HCV) polypeptide encoded by a particular domain of an HCV genome or immunogenic fragments of said polypeptide, and methods of preparing these compositions. Although the

claimed compositions do not exclude the presence of other polypeptides (as correctly stated by the Examiner in the Office Action), the requirement for an isolated immunogenic HCV polypeptide sufficiently set the presently claimed inventive subject matter apart from the intact viruses or whole viral preparations described in the cited references.

Since the cited references lack any teachings with regard to a key limitation of the claimed invention--i.e., isolated HCV polypeptides, whether the strains of NANBV disclosed in the prior arts are the same as HCV bears no significant relevancy to the issues. The cited references do not teach each and every limitation of the inventive subject matter as currently claimed and therefore could not have anticipated the present invention. Accordingly, Applicants respectfully request that the rejections under §102(b) be withdrawn.

Summary

Applicants submit that for the above-stated reasons the claims and specification comport with the requirements of 35 U.S.C. §102, and 112. Applicants respectfully request that the rejections be reconsidered and withdrawn, and a Notice of Allowance be issued.

Applicants also request that all future correspondences continue to be directed to Ms. Alisa A. Harbin, Esq. of Chiron Corporation at the following address:

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In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 223002006313. The

Assistant Commissioner is not, however, authorized to charge the cost of the issue fee to the Deposit Account.

Dated: August 2, 1999

Respectfully submitted,

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